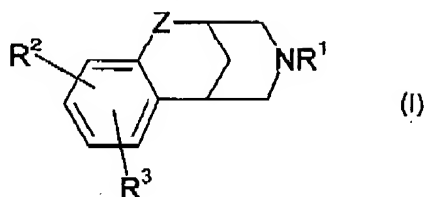


Patent Application 10/764,167
Attorney Docket No. PC10203C

IN THE CLAIMS (37 CFR 1.121 Revised)

1. (original) A compound of the formula



wherein Z is CH₂, C(=O) or CF₂;

R¹ is hydrogen, (C₁-C₈)alkyl, unconjugated (C₃-C₈)alkenyl, benzyl, XC(=O)R¹³ or -CH₂CH₂O-(C₁-C₄)alkyl;

R² and R³ are selected independently, from hydrogen, (C₂-C₈) alkenyl, (C₂-C₈) alkynyl, hydroxy, nitro, amino, halo, cyano, -SO_q(C₁-C₆)alkyl wherein q is zero, one or two, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂amino, CO₂R⁴, CONR⁵R⁶, SO₂NR⁷R⁸, C(=O)R¹³, XC(=O)R¹³, aryl-(C₀-C₃) alkyl or aryl-(C₀-C₃)alkyl-O- wherein said aryl is selected from phenyl and naphthyl, heteroaryl-(C₀-C₃)alkyl or heteroaryl-(C₀-C₃)alkyl-O-, wherein said heteroaryl is selected from five to seven membered aromatic rings containing from one to four heteroatoms selected from oxygen, nitrogen and sulfur, and X²(C₀-C₈)alkoxy-(C₀-C₈)alkyl, wherein X² is absent or X² is (C₁-C₆)alkylamino or [(C₁-C₆)alkyl]₂amino, and wherein the (C₀-C₈)alkoxy-(C₀-C₈)alkyl moiety of said X²(C₀-C₈)alkoxy-(C₀-C₈)alkyl contains at least one carbon atom, and wherein from one to three of the carbon atoms of said (C₀-C₈)alkoxy-(C₀-C₈)alkyl moiety may optionally be replaced by an oxygen, nitrogen or sulfur atom, with the proviso that any two such heteroatoms must be separated by at least two carbon atoms, and wherein any of the alkyl moieties of said (C₀-C₈)alkoxy-(C₀-C₈)alkyl may be optionally substituted with from two to seven fluorine atoms, and wherein one of the carbon atoms of each of the alkyl moieties of said aryl-(C₀-C₃)alkyl and said heteroaryl-(C₀-C₃)alkyl may optionally be replaced by an oxygen, nitrogen or sulfur atom, and wherein each of the foregoing aryl and heteroaryl groups may optionally be substituted with one or more substituents, preferably from zero to two substituents, independently selected from (C₁-C₆) alkyl optionally substituted with from one to seven fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from two to seven fluorine atoms, halo (e.g., chloro, fluoro, bromo or iodo), hydroxy, nitro, cyano, amino, (C₁-C₆) alkylamino and [(C₁-C₆) alkyl]₂ amino;

or R² and R³, together with the carbons to which they are attached, form a four to seven membered monocyclic, or a ten to fourteen membered bicyclic, carbocyclic ring, that can be saturated or unsaturated, wherein from one to three of the nonfused carbon atoms of said monocyclic rings, and from one to five of the carbon atoms of said bicyclic rings that are not part of the benzo ring shown in formula I, may optionally and independently be replaced by a nitrogen, oxygen or sulfur, and wherein said monocyclic and bicyclic rings may optionally be substituted with one or more substituents, preferably from zero to two substituents for the monocyclic rings

Patent Application 10/764,167
Attorney Docket No. PC10203C

and from zero to three substituents for the bicyclic rings; that are selected, independently, from (C₀-C₆) alkoxy-(C₀-C₆)alkyl-, wherein the total number of carbon atoms does not exceed six and wherein any of the alkyl moieties may optionally be substituted with from one to seven fluorine atoms; nitro, oxo, cyano, halo, hydroxy, amino, (C₁-C₆)alkylamino, [(C₁-C₆) alkyl]₂amino, phenyl and monocyclic heteroaryl wherein said heteroaryl is defined as in the definition of R² and R³ above:

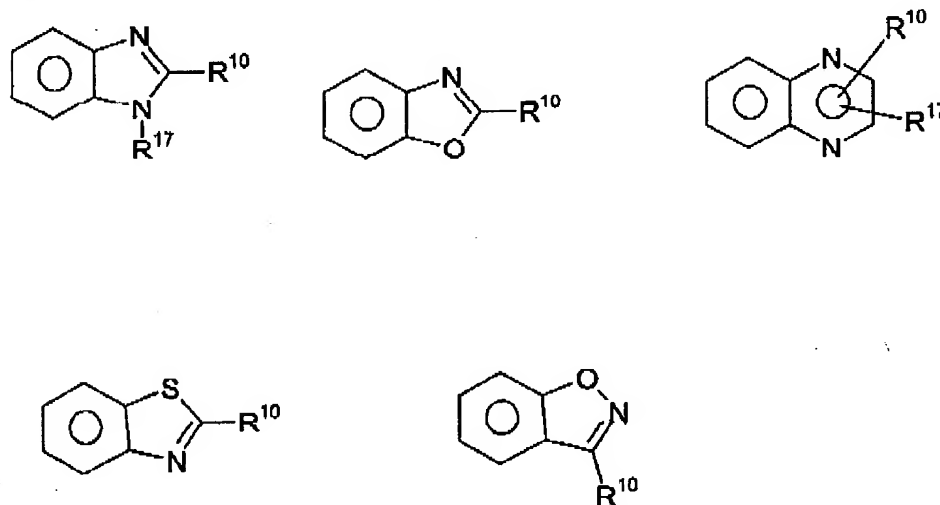
each R⁴, R⁵, R⁶, R⁷, R⁸ and R¹³ is selected, independently, from hydrogen and (C₁-C₆) alkyl, or R⁵ and R⁶, or R⁷ and R⁸ together with the nitrogen to which they are attached, form a pyrrolidine, piperidine, morpholine, azetidine, piperazine, -N-(C₁-C₆)alkylpiperazine or thiomorpholine ring, or a thiomorpholine ring wherein the ring sulfur is replaced with a sulfoxide or sulfone; and

each X is, independently, (C₁-C₆)alkylene;

with the proviso that: (a) at least one of R¹, R² and R³ must be the other than hydrogen, (b) when R² and R³ are hydrogen, R¹ cannot be methyl or hydrogen; and (c) no fluorine atom in any of the fluoro substituted alkyl or alkoxy moieties of R² and R³ can be attached to a carbon that is attached to a heteroatom;

or a pharmaceutically acceptable salt thereof;

2. (original) A compound according to claim 1, wherein R² and R³, together with the benzo ring of formula I, form a bicyclic ring system selected from the following:



wherein R¹⁰ and R¹⁷ are selected, independently, from hydrogen and (C₁-C₆)alkyl.

3. (original) A compound according to claim 1, wherein R² and R³ do not, together with the benzo ring of formula I, form a bicyclic or tricyclic ring system.

4. (original) A compound according to claim 1, wherein one or both of R² and R³ are -C(=O)R¹³ wherein R¹³ is (C₁-C₆)alkyl.

Patent Application 10/764,167
Attorney Docket No. PC10203C

5. (original) A compound according to claim 1, wherein one of R^2 and R^3 is $-COR^{13}$ wherein R^{13} is (C_1-C_8) alkyl or (C_1-C_3) alkyl optionally substituted with from one to seven fluorine atoms.

6. (original) A compound according to claim 1, wherein one of R^2 and R^3 is CF_3 , fluoro, cyano or C_2F_5 .

7. (original) A pharmaceutical composition for use in reducing nicotine addiction or aiding in the cessation or lessening of tobacco use in a mammal, comprising an amount of a compound according to claim 1 that is effective in reducing nicotine addiction or aiding in the cessation or lessening of tobacco use and a pharmaceutically acceptable carrier.

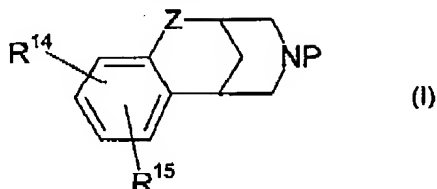
8. (original) A method for reducing nicotine addiction or aiding in the cessation or lessening of tobacco use in a mammal, comprising administering to said mammal an amount of a compound according to claim 1 that is effective in reducing nicotine addiction or aiding in the cessation or lessening of tobacco use.

9. (original) A pharmaceutical composition for treating a disorder or condition selected from inflammatory bowel disease, irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supramuscular palsy, chemical dependencies and addictions, headache, stroke, TBI, psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal, comprising an amount of a compound according to claim 1 that is effective in treating such disorder or condition and a pharmaceutically acceptable carrier.

10. (original) A method for treating a disorder or condition selected from inflammatory bowel disease, irritable bowel syndrome, spastic dystonia, chronic pain, acute pain, celiac sprue, pouchitis, vasoconstriction, anxiety, panic disorder, depression, bipolar disorder, autism, sleep disorders, jet lag, amyotrophic lateral sclerosis (ALS), cognitive dysfunction, hypertension, bulimia, anorexia, obesity, cardiac arrhythmias, gastric acid hypersecretion, ulcers, pheochromocytoma, progressive supramuscular palsy, chemical dependencies and addictions, headache, stroke, TBI, psychosis, Huntington's Chorea, tardive dyskinesia, hyperkinesia, dyslexia, schizophrenia, multi-infarct dementia, age related cognitive decline, epilepsy, including petit mal absence epilepsy, senile dementia of the Alzheimer's type (AD), Parkinson's disease (PD), attention deficit hyperactivity disorder (ADHD) and Tourette's Syndrome in a mammal, comprising administering to a mammal in need of such treatment an amount of a compound according to claim 1 that is effective in treating such disorder or condition.

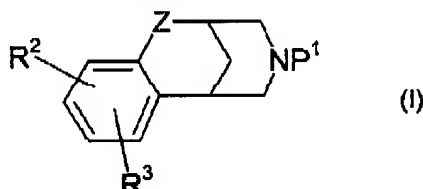
Patent Application 10/764,167
Attorney Docket No. PC10203C

11. (original) A compound of the formula



wherein Z is CH_2 , CF_3 or C(=O) ; P is hydrogen, methyl, COOR^{16} wherein R^{16} is $(\text{C}_1\text{-C}_8)$ alkyl, allyl or 2,2,2-trichloroethyl; $-\text{C(=O)NR}^5\text{R}^6$ wherein R^5 and R^6 are defined as in formula I above; $-\text{C(=O)H}$, $-\text{C(=O)(C}_1\text{-C}_8\text{)alkyl}$ wherein the alkyl moiety may optionally be substituted with from 1 to 3 halo atoms, preferably with from 1 to 3 fluoro or chloro atoms; benzyl or t-butoxycarbonyl (t-Boc), and R^{14} and R^{15} are selected, independently, from hydroxy, nitro, amino, $-\text{O(C}_1\text{-C}_8\text{)alkyl}$ and halo; with the proviso that R^{14} and R^{15} cannot both be hydrogen when P is hydrogen or methyl.

12. (original) A compound of the formula



wherein Z is CH_2 , CF_3 or C(=O) ; R^2 and R^3 are defined as in claim 2; and P^1 is COOR^{16} wherein R^{16} is allyl, 2,2,2-trichloroethyl or $(\text{C}_1\text{-C}_8)$ alkyl; $-\text{C(=O)NR}^5\text{R}^6$ wherein R^5 and R^6 are defined as in formula I above; $-\text{C(=O)H}$, $-\text{C(=O)(C}_1\text{-C}_8\text{)alkyl}$ wherein the alkyl moiety may optionally be substituted with from 1 to 3 halo atoms, preferably with from 1 to 3 fluoro or chloro atoms; benzyl, t-butoxycarbonyl (t-Boc), or trifluoroacetyl.

13. (New) A compound according to claim 1 selected from the group consisting of

11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;

11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;

1-[11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-ethanone;

1-[11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl]-1-propanone;

4-Fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carbonitrile;

5-Fluoro-11-azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-4-carbonitrile;

1-[11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-4-yl]-1-ethanone;

1-[11-Azatricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-4-yl]-1-propanone;

6-Methyl-7-thia-5,14-diazatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,5,8-tetraene;

Patent Application 10/764,167
Attorney Docket No. PC10203C

6-Methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
6,7-Dimethyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
5,7,14-Triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
7-Methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
5,11,18-Triazapentacyclo[14.3.1.0²,14.0⁴,12.0⁶,11]jicosa-2(14),3,5,12-tetraene;
7-Ethyl-6-methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
6-Methyl-7-propyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-
tetraene;
7-Ethyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
7-Butyl-6-methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
7-Isobutyl-6-methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-
tetraene;
7-Butyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
7-Isobutyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
5,11,18-Triazapentacyclo[14.3.1.0²,14.0⁴,12.0⁵,10]jicosa-2(14),3,10,12-tetraene;
5,6-Dimethyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
5-Ethyl-6-methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
5-Methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
6-Ethyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
8-Methyl-5-propyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-
tetraene;
5-Isobutyl-6-methyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-
tetraene;
5-Propyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
5-Isobutyl-5,7,14-triazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,6,8-tetraene;
6-(Trifluoromethyl)-7-thia-5,14-diazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-
tetraene;
5,8,15-Triazatetracyclo[11.3.1.0²,11.0⁴,9]heptadeca-2(11),3,5,7,9-pentaene;
7-Methyl-5,8,15-triazatetracyclo[11.3.1.0²,11.0⁴,9]heptadeca-2(11),3,5,7,9-pentaene;
6-Methyl-5,8,15-triazatetracyclo[11.3.1.0²,11.0⁴,9]heptadeca-2(11),3,5,7,9-pentaene;
6,7-Dimethyl-5,8,15-triazatetracyclo[11.3.1.0²,11.0⁴,9]heptadeca-2(11),3,5,7,9-pentaene;
7-Oxa-5,14-diazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;
6-Methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0²,10.0⁴,8]hexadeca-2(10),3,5,8-tetraene;

Patent Application 10/764,167
Attorney Docket No. PC10203C

6-Ethyl-7-oxa-5,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,5,8-tetraene;
6-Propyl-7-oxa-5,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,5,8-tetraene;
5-Methyl-7-oxa-6,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,5,8-tetraene;
5-Oxa-7,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,6,8-tetraene;
6-Methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,6,8-tetraene;
6-Ethyl-5-oxa-7,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,6,8-tetraene;
6-Propyl-5-oxa-7,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,6,8-tetraene;
7-Methyl-5-oxa-6,14-diazatetracyclo[10.3.1.0²,10⁴,8]hexadeca-2(10),3,6,8-tetraene;
4,5-Difluoro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
4-chloro-5-fluoro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
5-Chloro-4-fluoro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
4-(1-Ethynyl)-5-fluoro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
5-(1-Ethynyl)-4-fluoro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
4,5-Dichloro-11-azatricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene.
and pharmaceutically acceptable salts and optical isomers thereof.

14. (New) A compound according to claim 1 selected from the group consisting of 5,6-difluoro-11-aza-tricyclo[7.3.1.0²,7]trideca-2,4,6-triene;
11-benzyl-6-methoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
6-methoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-trien-6-ol;
6-fluoro-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-benzyl-5-methoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-benzyl-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-trien-5-ol;
5-methoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-trien-5-ol;
11-benzyl-5-difluoromethoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
5-difluoromethoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-benzyl-5-ethoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
5-ethoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
5-isopropoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;
11-benzyl-4-methoxy-11-aza-tricyclo[7.3.1.0²,7]trideca-2(7),3,5-triene;

Patent Application 10/764,167
Attorney Docket No. PC10203C

4-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-4-ol;
11-benzyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
4-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
3-nitro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-benzyl-5-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-fluoro-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5,7-dioxa-14-azatetracyclo[10.3.1.0^{2,10}.0^{4,8}]hexadeca-2(10),3,8-triene;
11-benzyl-6-bromo-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-benzyl-5-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
6-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
trifluoromethanesulfonic acid-11-benzyl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl ester;
5-(4-trifluoromethyl-phenyl)-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
5-(4-methoxy-phenyl)-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene-5-carboxylic acid methyl ester;
2-(11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-trien-5-yl)-propan-2-ol;
5-pyrrolidin-3-yl-11-aza-tricyclo[7.3.1.0^{2,7}]trideca-2(7),3,5-triene;
and pharmaceutically acceptable salts and optical isomers thereof.